507 Eugenia Avenue
Madison 5, Wisconsin
November 29, 1956

Dear Joe:

I was very pleased to get your surprise package yesterday (the voicewriter). Thank you very much for arranging this, and also for the good tidings in your letter, and the penicillin sample. (It behaves just like the commercial product in our test.) I am certainly not going to refuse your generous increase; I trust the arrangement is still governed by our original exchange of letters; for my own tax purposes, the 'stipend' is a retainer and fee for consultation services.

Unfortunately, something seems to be wrong with the machine, as I think you will hear from the quality of the attached record. Should I make arrangements to have it serviced locally, return it, or is it good enough to struggle along with it?

I have been preoccupied all day today with an idea for a "new" approach to pharmacal screening, which is so simple and direct it is hard for me to understand why it hasn't been exploited before. And while a number of precedents remotely approach it, I don't believe it has been. Briefly, it is to use the whole, normal target-organism itself as the raw material for making derivatives of its biochemical parts that might serve as specific antagonists to those parts. I have spelled this out more fully in the attached memorandum. I wish I could come out to talk ~~to~~ to you about this more fully, and perhaps more convincingly, but I just can't take the time right now. Any chance of your visiting Madison, as I have asked before?

I was thinking whether it would be better to publish this notion formally, or discuss it widely, but as with the DAP-suggestions, it did not take me long to decide that it would have a better chance of being promptly tested and exploited if I brought it directly to your attention. Please let me know if you can imagine going into this line in the foreseeable future, and if so I will keep my counsel on it while you explore its possibilities; if not, either because the idea seems implausible, or you are too heavily committed in other directions, please let me know so I can think what else to do. I am almost tempted to set up some trials in collaboration here, but I doubt if that would be very practical, except as a last resort.

Yours sincerely,

Joshua Lederberg

P.S. This whole idea is perhaps in the best traditions of Schmear-chemistry: what brings it into focus again is the development of techniques like paper chromatography for the empirical separation of many constituents with minimum effort. Now I suppose that natural products like coal tar have already been worked over sufficiently (via creosote) and there would be too many irrelevant inhibitors in the phenols, but think how many other natural products there are, cheap as sawdust, and almost untouched this way. I'm still fonder of the more specific angle (using the target organism itself); on the other hand, carbohydrate analogues are an almost untouched field, and products like cellulose and starch, and already-known derivatives like the oxidised cellulose, may be expected to give masses of biochemically-related and never-yet investigated derivatives. Have you any idea, for example, of the biological activity of a sulfonated glucuronic acid?

Thinking over what I would do first if I were a hundred organic chemists, I would try to develop reagents to introduce F (fluorine) in carbon-bound linkages. (Cf. fluorophenylalanine). Can you do this with elementary fluorine? But there's probably as much use in an unreasoned approach with any agent that comes to hand.

Yrs.